

Please amend claim 6 as follows:

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--6. (Amended) A method according to claim 1, wherein the detection method comprises PCR amplification of the *GH1* gene of the individual using (a) a *GH1* gene-specific fragment, being a fragment unique to the *GH1* gene whose sequence is not found in the four other paralogous (non-*GH1*) genes in the GH cluster, and (b) one or more *GH1* gene-specific primers which cannot bind to the homologous flanking regions in the four other paralogous (non-*GH1*) genes in the GH cluster.

Please amend claim 7 as follows:

a⁴
--7. (Amended) A method according to claim 1, wherein the detection method comprises PCR amplification of the entire *GH1* gene of the individual and nested PCR of overlapping constituent fragments of the *GH1* gene of the individual. --

Please amend claim 8 as follows:

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--8. (Amended) A method according to claim 1, wherein the detection method comprises PCR amplification of all or a fragment of genomic DNA spanning the Locus Control Region of the *GH1* gene.--

Please amend claim 9 as follows:

a⁶
--9. (Amended) A method according to claim 1, wherein the detection method comprises mutational screening of all or a fragment of the individual's *GH1* gene by DHPLC.--

Please amend claim 11 as follows:

--11. (Amended) A detection method according to claim 10, which detection method further comprises the use of one or more primer(s) selected from:

CTC CGC GTT CAG GTT GGC (GH1DF);
AGG TGA GCT GTC CAC AGG (GH1DR);
GGG CAA CAG TGG GAG AGA AG (GH2DF);
CCT CCA GGG ACC AGG AGC (GH2DR);
CAT GTA AGC CCA GTA TTT GGC C (GH3DF);
CTG AGC TCC TTA GTC TCC TCC TCT (GH3DR);
GAC TTT CCC CCG CTG GGA AA (GH4DF);
GGA GAA GGC ATC CAC TCA CGG (GH4DR);
TCA GAG TCT ATT CCG ACA CCC (GH5DF);
GTG TTT CTC TAA CAC AGC TCT C (GH5DR);
TCC CCA ATC CTG GAG CCC CAC TGA (GH6DF);
CGT AGT TCT TGA GTA GTG CGT CAT CG (GH6DR);
TTC AAG CAG ACC TAC AGC AAG TTC G (GH7F);
CTT GGT TCC CGA ATA GAC CCC G (GH7DR);
GTGCCCCAAGCCTTTCCC (LCR15: 1159-1177);
TGTCAGATGTTTCAGTTCATGG (LCR13: 1391-1412);
CCTCAAGCTGACCTCAGG (LCR25: 1346-1363);
GATCTTGGCCTAGGCCTCG (LCR23: 1584-1602);
LCR 5A (5' CCAAGTACCTCAGATGCAAGG 3');
LCR 3.0 (5' CCTTAGATCTTGGCCTAGGCC 3');
LCR 5.0 (5' CCTGTCACCTGAGGATGGG 3');
LCR 3.1 (5' TGTGTTGCCTGGACCCTG 3');
LCR 3.2 (5' CAGGAGGCCTCACAAGCC 3')

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LCR 3.3 (5' ATGCATCAGGGCAATCGC 3');
GH1G5 (5' GGTACCATGGCTACAGGTAAGCGCC 3');
GH1G3 (5' CTCGAGCTAGAAGCCACAGCTGCCC 3');
BGH3 (5' TAGAAGGCACAGTCGAGG 3');
GH1R5 (5' ATGGCTACAGGCTCCCGG 3'); and
GH1R3 (5' CTAGAAGCCACAGCTGCCC 3')---

Please amend claim 12 as follows:

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--12. (Amended) A variant of GH1, which differs from GH1 and is detected by or is detectable by a method according to claim 1 but was not detected by methods used hitherto, such as those reliant on patient selection criteria based primarily on absolute height.--

Please amend claim 14 as follows:

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--14. (Amended) A variant of GH1 according to claim 12 comprising a missense mutation.--

Please amend claim 15 as follows:

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--15. (Amended) A variant of GH1 according to claim 12 comprising a silent mutation which affects the activity of the signal peptide.--

Please amend claim 17 as follows:

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Q11

--17. (Amended) A protein or amino acid sequence encoded by a variant of GH1 according to claim 12.--

Please amend claim 21 as follows:

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--21. (Amended) A screening method for screening an individual suspected of GH dysfunction, which screening method comprises the steps of:

(a) obtaining a test sample comprising a nucleotide sequence of the human *GH1* gene from the individual; and

(b) comparing a region of the sequence obtained from the test sample with the corresponding region of a predetermined sequence

wherein the predetermined sequence is selected from a variant of *GH1* according to claim 12.--

Amend claim 24 as follows:

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--24. (amended) A screening method according to claim 21, comprising:

(a) obtaining a first test sample from an individual; and

(b) comparing the *GH1* gene or *GH1* transcript, or fragment therefrom (eg cDNA), in the first test sample to the corresponding gene, transcript or fragment of a *GH1* variant obtainable from a second test sample derived from an individual exhibiting the following criterion:

(i) growth failure defined as a growth pattern [delineated by a series of height measurements; Brook CDG (Ed) Clinical Paediatric Endocrinology 3rd Ed, Chapter 9, p141 (1995, Blackwell Science)] which, when plotted on a standard height chart [Tanner et al Arch. Dis. Child 45 755-762 (1970)], predicts an adult height for the individual which is outside the individual's estimated target adult height range, the

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estimate being based upon the heights of the individual's
parents.--

Amend claim 26 as follows:

GH4
--26. (amended) A screening method according to
claim 21 in which simultaneous screens are used either for
multiple known mutations or for all possible mutations by
hybridization of a labelled sample of DNA (cDNA or genomic DNA
derived from the individual) to micro-arrays of mutation-
specific oligonucleotide probes immobilised on a solid
support.--

Amend claim 28 as follows:

GH15
--28. (amended) A kit suitable for use in carrying
out a screening method according to claim 21, which kit
comprises:
(a) an oligonucleotide having a nucleic acid sequence
corresponding to a region of a GH1 variant, which region
incorporates at least one variation from the corresponding
wild-type hGH gene sequence; and/or
(b) an oligonucleotide having a nucleic acid sequence
corresponding to the wild-type hGH gene sequence in the region
specified in (a); and, optionally,
(c) one or more reagents suitable for carrying out PCR for
amplifying desired regions of the individual's DNA.--

Cancel claim 29.--

Q 16
--30. (amended) A kit according to claim 28, wherein kit component (a) comprises a plurality of said oligonucleotides immobilised on a solid support.--

--31. (amended) A kit suitable for use in carrying out a detection method in which the variant is at least one of the variants claimed in claim 12.--

Amend claim 32 as follows:

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--32. (amended) A screening method for screening an individual suspected of GH dysfunction, which screening method comprises the steps of:

- (a) obtaining a test sample comprising an amino acid sequence encoded by the human *GH1* gene of the individual; and
- (b) analysing the test sample for the presence of a GH variant wherein the GH variant is selected from those according to claim 17.--

Amend claim 34 as follows:

Q 18
--34. (amended) An isolated, purified or recombinant nucleic acid sequence selected from:

- (a) a sequence comprising a variant of *GH1* according to claim 12 or
- (b) a sequence substantially homologous to or that hybridises to sequence (a) under stringent conditions; or
- (c) a sequence substantially homologous to or that hybridizes under stringent conditions to the sequence (a) or (b) but for the degeneracy of the genetic code; or

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(d) an oligonucleotide specific for any of the sequences (a),
(b) or (c).--

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--37. (amended) A process for preparing a variant
of GH1 according to claim 12, which process comprises:
(i) culturing a host cell; and
(ii) recovering from the culture medium the variant of GH1
thereby produced.--

Amend claim 38 as follows:

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--38. (amended) An amino acid sequence encoded or
expressed by a sequence, vector, or cell as defined in claim
34 in culture medium.--

Amend claim 39 as follows:

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--39. (amended) A composition comprising a variant
of GH1 or a GH variant according to claim 12; respectively, in
association with a pharmaceutically acceptable carrier
therefor.--

Amend claim 40 as follows:

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--40. (amended) Use of a variant of GH1 or a GH
variant according to claim 12, respectively, for a
therapeutic, diagnostic or detection method.--

Cancel claim 42.

Cancel claim 43.

Amend claim 44 as follows: